

10/661,088

CIP of PCT/1303/04573
III a us practice

029849-0206

WHAT IS CLAIMED IS:

1. A method for the prophylaxis or treatment of a HBV infection in a subject, comprising
administering to a subject in need of such treatment a therapeutically effective amount of at least one pharmacologically acceptable oligonucleotide at least 10 nucleotides in length, wherein the anti-HBV activity of said oligonucleotide occurs principally by a non-sequence complementary mode of action.
2. The method of claim 1, wherein said subject is a human.
3. An antiviral pharmaceutical composition comprising
a therapeutically effective amount of at least one pharmacologically acceptable, antiviral oligonucleotide at least 10 nucleotides in length, wherein said composition is approved for use in humans against HBV and the antiviral activity of said oligonucleotide occurs principally by a non-sequence complementary mode of action; and
a pharmaceutically acceptable carrier.
4. The antiviral pharmaceutical composition of claim 3, adapted for delivery by oral ingestion.
5. The antiviral pharmaceutical composition of claim 3, adapted for delivery enterally.
6. The antiviral pharmaceutical composition of claim 3, adapted for delivery by injection.
7. The antiviral pharmaceutical composition of claim 3, adapted for delivery by inhalation.
8. The antiviral pharmaceutical composition of claim 3, adapted for delivery topically.

9. The antiviral pharmaceutical composition of claim 3, wherein said composition further comprises a delivery system.
10. The antiviral pharmaceutical composition of claim 3, wherein said composition further comprises a liposomal formulation.
11. The antiviral pharmaceutical composition of claim 3, wherein said composition further comprises at least one other antiviral drug in combination.
12. A kit comprising at least one anti-HBV oligonucleotide or anti-HBV oligonucleotide formulation in a labeled package, wherein said oligonucleotide is at least 10 nucleotides in length, the anti-HBV activity of said oligonucleotide occurs principally by a non-sequence complementary mode of action, and the label on said package indicates that said anti-HBV oligonucleotide can be used against HBV.
13. The kit of claim 12, wherein said kit is approved by a regulatory agency for use in humans.
14. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein said at least one antiviral oligonucleotide comprises at least one antiviral randomer oligonucleotide.
15. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein said oligonucleotide is not complementary to any portion of the genomic sequence of HBV.
16. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein said formulation has an IC_{50} for HBV of 0.10 μ M or less.
17. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein said oligonucleotide is at least 40 nucleotides in length.

18. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein each said oligonucleotide comprises at least one modification to its chemical structure.
19. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein each said oligonucleotide comprises at least one phosphorothioated linkage.
20. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein each said oligonucleotide comprises at least one phosphorothioated linkage and is in a formulation comprising a delivery system.
21. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein each said oligonucleotide comprises at least one 2'- modification to the ribose moiety.
22. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein each said oligonucleotide comprises at least one methylphosphonate linkage.
23. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein each said oligonucleotide comprises at least one phosphorodithioated linkage.
24. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein each said oligonucleotide comprises at least one phosphorodithioated linkage and is in a formulation comprising a delivery system.
25. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein said oligonucleotide is a ~~concatemer consisting of two or more~~ oligonucleotide sequences joined by a linker.
26. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein said oligonucleotide is linked or conjugated at one or more nucleotide residues, to a molecule modifying the characteristics of the oligonucleotide to obtain one or more characteristics selected from the group

consisting of higher stability, lower serum interaction, higher cellular uptake, higher viral protein interaction, an improved ability to be formulated for delivery, a detectable signal, higher antiviral activity, better pharmacokinetic properties, specific tissue distribution, lower toxicity.

27. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein said oligonucleotide is double stranded.
28. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein said oligonucleotide binds to one or more viral components.
29. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, wherein at least a portion of the sequence of said oligonucleotide is derived from a viral genome.
30. The method, pharmaceutical composition, or kit of claim 1, 3, or 12, comprising a mixture of at least two different antiviral oligonucleotides.
31. The method, pharmaceutical composition, or kit of claim 30, wherein a plurality of said different oligonucleotides are at least 10 nucleotides in length.
32. The method, pharmaceutical composition, or kit of claim 30, wherein a plurality of said different oligonucleotides are at least 40 nucleotides in length.
33. A method for selecting an antiviral oligonucleotide for use as an anti-HBV agent, comprising
 - synthesizing a plurality of different oligonucleotides, wherein at least one of said different oligonucleotides is at least 29 nucleotides in length;
 - testing said oligonucleotides for activity in inhibiting the ability of HBV to produce infectious virions,
 - selecting a said oligonucleotide having a pharmaceutically acceptable level of activity for use as an anti-HBV agent.

34. The method of claim 33, wherein said different oligonucleotides comprise randomers of different lengths.
35. The method of claim 33, wherein said different oligonucleotides comprise a set of oligonucleotides of different length, each oligonucleotide in said set comprising the sequence of the shortest oligonucleotide in said set.
36. The method of claim 33, wherein said different oligonucleotides comprise a plurality of oligonucleotides comprising a randomer segment at least 6 nucleotides in length.
37. The method of claim 33, wherein said different oligonucleotides are not complementary to any HBV mRNA sequence.
38. A method for the prophylaxis or treatment of a HBV infection in a subject, comprising
administering to a subject in need of such treatment a therapeutically effective amount of at least one pharmacologically acceptable oligonucleotide randomer at least 10 nucleotides in length, wherein the anti-HBV activity of said randomer occurs principally by a non-sequence complementary mode of action.